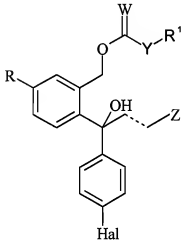
AMENDMENTS TO THE CLAIMS

Listing of Claims:

1. (Currently amended): A method for the isolation and purification of a compound having the formula



(IV)

wherein R is cyano ~~or a group which may be converted to a cyano group~~, halogen, CF_3-$(CF_2)_n$-SO_2-O-, -CHO, $-CH_2NO_2$, $-CH_2Cl$, $-CH_2Br$, $-CH_3$, $-COOR^6$, $-CONR^6R^7$, or a group of formula

(VII), wherein

n is 0-8,

R^6 and R^7 are independently selected from optionally substituted C_{1-6}-alkyl, optionally substituted aryl-C_{1-6}-alkyl, and optionally substituted aryl,

Z' in formula (VII) is O or S,

R^8 and R^9 are independently hydrogen or C_{1-6}-alkyl or R^8 and R^9 together form a C_{2-5}-alkylene chain thereby forming a spiro ring,

R^{10} is hydrogen or C_{1-6}-alkyl, and

R^{11} is hydrogen, C_{1-6}-alkyl, a carboxy group, or a precursor group thereto, or R^{10} and R^{11} together form a C_{2-5}-alkylene chain thereby forming a spiro ring,

the dotted line represents a double or single bond,

Hal is halogen,

Z is a dimethylaminomethyl group ~~or Z is a group which may be converted to a dimethylaminomethyl group~~, $-CH_2$-L, $-CH_2-NO_2$, cyano, aldehyde, $-CH_2$-O-Pg, $-CH_2-NPg_1Pg_2$, $-CH_2-NMePg_1$, $-CO-N(CH_3)_2$, $-CH(A^1R^{12})(A^1R^{13})$, $-(A^1R^{14})(A^2R^{15})(A^3R^{16})$, $-COOR^{17}$, or $-CH=CH-R^{18}$, wherein

Pg is a protection group for an alcohol group,

Pg_1 and Pg_2 are each independently a protection group for an amino group,

R^{12} and R^{13} are independently C_{1-6}-alkyl, C_{2-6}-alkenyl, C_{2-6}-alkynyl, or an optionally alkyl-substituted aryl or aralkyl group, or R^{12} and R^{13} together form a chain of 2 to 4 carbon atoms,

each of R^{14} - R^{18} are independently C_{1-6}-alkyl, C_{2-6}-alkenyl, C_{2-6}-alkynyl, or optionally C_{1-6}-alkyl-substituted aryl or aryl-C_{1-6}-alkyl,

A^1, A^2 and A^3 are independently O or S, and

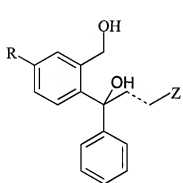
L is a leaving group,

W is O or S,

Y is a bond, O, S or NH,

and R^1 is C_{1-10}-alkyl, C_{2-10}-alkenyl or C_{2-10}-alkynyl all of which may optionally be substituted with one or more substituents selected from C_{1-10}-alkoxy, C_{1-10}-alkylthio, ~~hydroxy,~~ halogen, ~~amino,~~ nitro, cyano, ~~C_{1-10}-alkylamino,~~ di-(C_{1-10}-alkyl)amino, aryl, aryloxy, arylthio and heteroaryl, or R^1 is aryl, wherein any of the aryl and heteroaryl groups may optionally be substituted one or more times with substituents selected from C_{1-10}-alkyl, C_{2-10}-alkenyl, C_{2-10}-alkynyl, C_{1-10}-alkoxy, C_{1-10}-alkylthio, ~~hydroxy,~~ halogen, ~~amino,~~ nitro, cyano, ~~C_{1-10}-alkylamino~~ and di-(C_{1-10}-alkyl)amino, or a salt thereof,

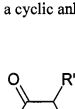
and/or a diol of formula



(II)

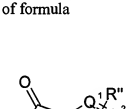
wherein R, Z, Hal and the dotted line are as defined above, or a salt thereof, from a mixture containing the compound of formula (IV) and the diol of formula (II), comprising:

a) reacting said mixture containing the compound of formula (IV) and the diol of formula (II) with a cyclic anhydride or imide of formula



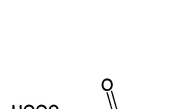
(Ia)

or



(Ib)

or



(Ic)

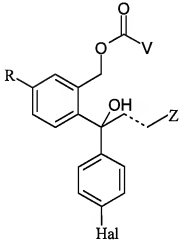
wherein X is $-(CHR''')_n-$, wherein n is 0-2;

and R', R'', and R''' are independently selected from hydrogen, C_{1-6}-alkyl, C_{1-6}-alkoxy, aryloxy, C_{1-6}-acyloxy, and aryl-CO-O, wherein each aryl may be substituted with C_{1-6}-alkyl, or R' and R'' in an anhydride of formula (Ia) together are $-O-CR^4R^5-O-$, wherein R^4 and R^5 are independently hydrogen or C_{1-6}-alkyl, or R' and R'' in an anhydride of formula (Ib) are adjacent and together with the two carbon atoms to which they are attached form a benzene ring;

one of Q^1 and Q^2 is nitrogen and the other is carbon, or both are carbon;

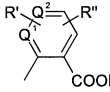
A is C_{1-6}-alkylene, phenylene, or naphthylene wherein the C_{1-6}-alkylene, phenylene, or naphthylene groups may optionally be substituted one or more times with C_{1-6}-alkyl;

to form a mixture of the compound of formula (IV) and an ester having the formula

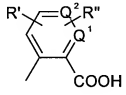


(V)

wherein R, Z and Hal are as defined above and V is –CHR'-X-CR''-COOH, -X-CHR''-CO-NH-A-COOH, - CHR''-X-CO-NH-A-COOH,



or



wherein R', R'', X, and A are as defined above;

b) separating the compound of formula (IV) from the ester of formula (V) by a method selected from the group consisting of:

i) allowing the acid of formula (V) or a salt thereof to precipitate from the reaction mixture, and separating the precipitate of the compound of formula (V) or a salt thereof from the reaction mixture, optionally followed by isolation of the compound of formula (IV) or a salt thereof from the reaction mixture;

ii) partitioning between an organic solvent and an aqueous solvent whereby the compound of formula (IV) will be dissolved in the organic phase whereas the compound of formula (V) will be dissolved in the aqueous phase, separating the phases, and optionally isolating the compound of formula (IV) or a salt thereof and/or isolating the compound of formula (V) or a salt thereof; and

iii) adsorbing the compound of formula (V) on a basic resin, separating the solvent containing the compound of formula (IV) from the resin, desorbing the compound of formula (V) from the basic resin, and optionally isolating the compound of formula (IV) or a salt thereof and/or isolating the compound of formula (V) or a salt thereof.

2. (Previously presented): The method according to claim 1, wherein the separation of the compound of formula (IV) from the ester of formula (V) is performed by allowing the acid of formula (V) or a salt thereof to precipitate from the reaction mixture, and separating the precipitate of the compound of formula (V) of a salt thereof from the reaction mixture, optionally followed by isolation of the compound of formula (IV) or a salt thereof from the reaction mixture.

3. (Previously presented): The method according to claim 1, wherein R', R'', and R''' are independently selected from hydrogen and C_{1-6}-alkyl, and Q^1 and Q^2 are both carbon.

4. (Previously presented): The method according to claim 1, wherein the S-enantiomer of the compound of formula (V) or a mixture of enantiomers of the compound of formula (V) comprising more than 50% of the S-enantiomer of the compound of formula (V) is separated from the R-enantiomer of the acyl derivative of formula (IV) or from a mixture of enantiomers of the acyl derivative of formula (IV) comprising more than 50% of the R-enantiomer of the acyl derivative of formula (IV).

5. (Original): The method according to claim 4 wherein the S-enantiomer of the compound of formula (V) is separated from the R-enantiomer of the acyl derivative of formula (IV) or from a mixture of enantiomers of the acyl derivative of formula (IV) comprising more than 50% of the R-enantiomer of the acyl derivative of formula (IV).

6. (Original): The method according to claim 5 wherein the S-enantiomer of the compound of formula (V) is separated from the R-enantiomer of the acyl derivative of formula (IV).

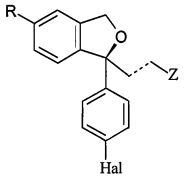
7. (Previously presented): The method according to claim 1, wherein the S-enantiomer of the acyl derivative of formula (IV) or a mixture of enantiomers of the acyl derivative of formula (IV) comprising more than 50% of the S-enantiomer of the acyl derivative of formula (IV) is separated from the R-enantiomer of the compound of formula (V) or from a mixture of enantiomers of the compound of formula (V) comprising more than 50% of the R-enantiomer of the compound of formula (V).

8. (Original): The method according to claim 7 wherein the S-enantiomer of the acyl derivative of formula (IV) is separated from the R-enantiomer of the compound of formula (V) or

from a mixture of enantiomers of the compound of formula (V) comprising more than 50% of the R-enantiomer of the compound of formula (V).

9. (Original): The method according to claim 8 wherein the S-enantiomer of the acyl derivative of formula (IV) is separated from the R-enantiomer of the compound of formula (V).

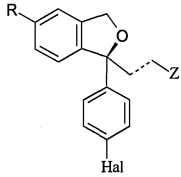
10. (Previously presented): The method according to claim 4, wherein the compound of formula (V) is obtained in the form of the S-enantiomer, and wherein R is optionally converted to cyano, Z is optionally converted to a dimethylaminomethyl group, Hal is optionally converted to fluoro, and/or a dotted line representing a double bond is optionally converted to a single bond, in any order, followed by conversion of the compound of formula (V) to escitalopram or a derivative thereof having the formula



(VI)

wherein R, Z and Hal are as defined above, by treatment with a base, optionally followed by, in any order, conversion of R to a cyano group, conversion of Z to a dimethylaminomethyl group, conversion of Hal to fluoro, and conversion of a dotted line representing a double bond to a single bond; optionally followed by conversion of escitalopram or a derivative of formula (VI) to a salt thereof.

11. (Previously presented): The method according to claim 7, wherein the compound of formula (IV) is obtained in the form of the S-enantiomer, and wherein R is optionally converted to cyano, Z is optionally converted to a dimethylaminomethyl group, Hal is optionally converted to fluoro and/or a dotted line representing a double bond is optionally converted to a single bond, in any order, followed by conversion of the compound of formula (IV) to escitalopram or a derivative thereof having the formula



(VI)

wherein R, Z and Hal are as defined above, by treatment with a base, optionally followed by, in any order, conversion of R to cyano, conversion of Z to a dimethylaminomethyl group, conversion of Hal to fluoro, and conversion of a dotted line representing a double bond to a single bond; optionally followed by conversion of escitalopram or a derivative of formula (VI) to a salt thereof.

12. (Previously presented): The method according to claim 10, wherein the basic ring closure is carried out by treatment with a base.

13. (Previously presented): The method according to claim 1, wherein Hal is fluoro and R is halogen or cyano.

14. (Previously presented): The method according to claim 1, wherein the dotted line represents a single bond.

15. (Previously presented): The method according to claim 1, wherein Z is a dimethylaminomethyl group or a group that may be converted to a dimethylaminomethyl group.

16. (Previously presented): The method according to claim 1, wherein the cyclic anhydride is a compound of formula (Ia).

17. (Previously presented): The method according to claim 16, wherein the cyclic anhydride is succinic anhydride or glutaric anhydride.

18. (Previously presented): The method according to claim 1, wherein the cyclic anhydride is a compound of formula (Ib).

19. (Previously presented): The method according to claim 18, wherein the cyclic anhydride is phthalic acid anhydride.

20. (Previously presented): The method according to claim 1, wher ein the imide is a compound of formula (Ic).

21. (Original): The method according to claim 20 wherein the imide is N-phenyl-succinimide substituted in the phenyl ring with a carboxy group.

22. (Previously presented): The method according to claim 1, wherein Y in the compound of formula (IV) is a bond.

23. (Previously presented): The method according to claim 1, wherein Y in the compound of formula (IV) is O or S.

24. (Original): The method according to claim 23 wherein Y in the compound of formula (IV) is O.

25. (Previously presented): The method according to claim 1, wherein Y in the compound of formula (IV) is NH.

26. (Previously presented): The method according to claim 1, wherein R^1 is selected from C_{1-4}-alkyl, C_{2-4}-alkenyl and C_{2-4}-alkynyl all of which may optionally be substituted one or more times with substituents selected from C_{1-4}-alkoxy, C_{1-4}-alkylthio, hydroxy, halogen, amino, nitro, cyano, C_{1-4}-alkylamino and di-(C_{1-4}-alkyl)amino.

27. (Original): The method according to claim 26 wherein R^1 is selected from C_{1-3}-alkyl, C_{2-3}-alkenyl and C_{2-3}-alkynyl all of which may optionally be substituted one or more times with substituents selected from C_{1-3}-alkoxy, C_{1-3}-alkylthio, hydroxy, halogen, amino, nitro, cyano, C_{1-3}-alkylamino and di-(C_{1-3}-alkyl)amino.

28. (Original): The method according to claim 26 wherein R^1 is C_{1-4}-alkyl.

29. (Original): The method according to claim 27 wherein R^1 is C_{1-3}-alkyl.

30. (Previously presented): The method of claim 29, wherein R^1 is methyl, ethyl, or propyl.

31. (Previously presented): The method according to claim 1, wherein the mixture of the compound of formula (IV) and the diol of formula (II) is prepared by selective enzymatic acylation or selective enzymatic deacylation.

32. (Previously presented): A method for the manufacture of escitalopram, comprising the method of claim 1.

33. (Previously presented): The method according to claim 12, wherein the base is selected from alkoxides, hydrides, or amines.

34. (Previously presented): The method according to claim 33, wherein the base is selected from $KOC(CH_3)_3$, NaH, triethylamine, ethyldiisopropylamine, and pyridine.

35. (Previously presented): The method according to claim 11, wherein the basic ring closure is carried out by treatment with a base.

36. (Previously presented): The method according to claim 35, wherein the base is selected from alkoxides, hydrides, or amines.

37. (Previously presented): The method according to claim 36, wherein the base is selected from $KOC(CH_3)_3$, NaH, triethylamine, ethyldiisopropylamine, and pyridine.

38. (Previously presented): The method according to claim 13, wherein R is cyano.

39. (Previously presented): The method according to claim 15, wherein Z is a dimethylaminomethyl group.

40. (Previously presented): The method according to claim 30, wherein R^1 is propyl.

41. (New): The method according to claim 1, wherein Pg is a trialkylsilyl group, benzyl group, or tetrahydropyranyl group (THP).

42. (New): The method according to claim 1, wherein Pg_1 and Pg_2 are independently aralkyl or $-SO_2-R^0$, where R^0 is alkyl, aralkyl, aryl or aryl substituted with alkyl, or Pg_1 and Pg_2 together with the N atom to which they are attached form an optionally substituted phthalimide group.